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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER	
BASI, N	
ART UNIT	**PAPER NUMBER**
1646	20

DATE MAILED: 09/13/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

PTO-90C (Rev.11/00)

1- File Copy

Office Action Summary

Application No.	Applicant(s)
09/057,150	CLARY, DOUGLAS
Examiner	**Art Unit**
Nirmal S. Basi	1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Mar 21, 2001* .

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *23-29* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *23-29* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

1. Amendment filed 3/21/00 has been entered.

Response to Amendment

2. Applicant asserts there is a well established utility for the claimed invention. Applicants states:

a. GDNF activates C-RET

b. Biological pathway governing C-RET is involved in neuronal survival

c. C-RET is implicated in development and survival of enteric, sympathetic and sensory neurons upon stimulation by the ligand GDNF

d. GDNF is a ligand for c-RET and C-RET is involved in neuronal cell survival

e. GDNF promotes the formation of a physical complex between GDNR-α and the orphan tyrosine kinase receptor RET, thereby inducing its tyrosine phosphorylation

f. Since GDNF promotes the survival and phenotype of central dopaminergic, noradrenergic and motor neurons, and GDNF is a ligand for C-RET, a well established utility for the instant invention is mediation of GDNF's effects on dopaminergic, noradrenergic and motor neurons

g. Over expression of C-RET is implicated in cancers and compounds that inhibit C-RET function as possible anti-cancer agents.

Pertaining to the utilities of instant invention are specific, Applicant states:

h. Because RPTKs control a variety of cellular functions, any alteration in the normal function of an RPTK can result in an abnormal condition in an organism and the determining the function of individual receptors is important for designing compounds that will prevent or treat these diseases

I. Claimed invention controls the survival of neurons with a compound that modulates C-RET function, a class of diseases that can be treated is neurodegenerative diseases such as Parkinson's disease

j. GDNF is a ligand that is known to interact with C-RET to induce tyrosine phosphorylation, and there is a real world use for identifying such ligands.

Applicants arguments have been fully considered but not found persuasive.

The specification discloses the **C-RET is an "orphan receptor"** (page 16, lines 11-16). The specification further discloses, "It is called a an orphan receptor because no ligand has been identified which directly activates it" (page 16, 20-21). The specification further states, "In addition, the **term "orphan receptor" as used herein refers to an RPTK without a known function"**, see page 16, lines 21-23. The specification clearly states that C-RET is an orphan receptor without a known function.

Although GDNF may promote tyrosine phosphorylation of C-RET there is no showing of what specific role the phosphorylated/non phosphorylated C-RET plays in survival of enteric, sympathetic and sensory neurons. The knowledge that GDNF binds C-RET does not give it

utility. Further, there is no showing that GDNF promotes the survival and phenotype of central dopaminergic, noradrenergic and motor neurons via its interaction with for C-RET. The specification nor prior art discloses that all proteins that interact with GDNF promotes the survival and phenotype of central dopaminergic, noradrenergic and motor neurons. There is no showing of what is the specific biological pathway governing C-RET and how it is specifically involved in neuronal survival. There is no shown of what specific cancers result as an over expression of C-RET and no compounds disclosed that inhibit C-RET function as possible anti-cancer agents. Examiner agrees RPTKs probably control a variety of cellular functions, any alteration in the normal function of an RPTK can result in an abnormal condition in an organism, but so can the alteration of the normal function non RPTKs. The utilities of instant invention are specific only when the function of individual receptor is known, and then they can be important for designing compounds that will prevent or treat known diseased involved in receptor dysfunction. Applicant does not any data showing that any specific neurodegenerative disease can be treated by modulating C-RET function, or what C-RET function has to be modulated to treat a neurodegenerative disease such as Parkinson's disease. Further, although, GDNF interacts with C-RET to induce tyrosine phosphorylation, and there is a no real world use for identifying such ligands without knowing the specific function of C-RET.

The utilities are not considered to be specific and substantial because the specification fails to disclose any particular function or biological significance for the C-RET of the instant invention. C-RET, is said to have a potential function based upon its phosphorylation by

GDNF. After further research, a specific and substantial credible utility might be found for the claimed C-RET. This further characterization, however, is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete.

The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-tumor activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. §101, which requires that an invention must have either an immediately apparent or fully disclosed "real world" utility. The court held that:

> The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. . . . [u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field. . . . a patent is not a hunting license. . . .[i]t is not a reward for the search, but compensation for its successful conclusion.

Claims of instant invention are drawn to a method of C-RET, as yet, undetermined function or biological significance. There is no evidence of record or any line of reasoning that would support a conclusion that the C-RET of the instant application was, as of the filing date, useful for "diagnosis, prevention, and treatment of disease", such as cancers etc. Until

some actual and specific significance can be attributed to C-RET, one of ordinary skill in the art would be required to perform additional experimentation in order to determine how to use the claimed invention. Thus, there was no immediately apparent or "real world" utility as of the filing date.

The C-RET of the instant invention may share some structural similarity to other orphan RPTKs disclosed on page 16 of the specification. Some of the other orphan RPTKs may also be phosphorylated by GDNF, but the phosphorylation of an orphan RPTKs does not disclose its biological function. GDNF may not even be the natural ligand for C-RET. In the absence of knowledge of the biological significance of C-RET, there is no immediately evident patentable use for the methods of instant invention. To employ C-RET of the instant invention in any of the disclosed methods would clearly be using it as the object of further research. Such a use has been determined by the courts to be a utility which, alone, does not support patentability. Since the instant specification does not disclose a credible "real world" use for C-RET, then the claimed invention as disclosed does not meet the requirements of 35 U.S.C. §101 as being useful.

In conclusion, the utilities asserted by Applicant are not specific or substantial. Since no specific function of C-RET is known, and the hypothesized function is based entirely on conjecture, the asserted utilities are not specific C-RET, but rather are based on its ability to br phosphorylated by GDNF. Neither the specification nor the art of record disclose C-RET being useful to identify drugs that affect said protein and modulate its activity. Similarly,

neither the specification nor the art of record disclose any instances where disorders can be effected by interfering with the activity using C-RET. Thus the corresponding asserted utilities are essentially methods of using C-RET to identify disease states associated with C-RET disfunction and as targets for drug discovery. Therefore the asserted utilities are essentially methods of testing for or for potentially treating unspecified, undisclosed diseases or conditions, which does not define a "real world" context of use. Treating or testing for compounds that interact with C-RET which may be implicated in an unspecified, undisclosed disease or condition would require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use. Since neither the specification nor the art of record disclose any activities or properties that would constitute a "real world" context of use for C-RET and the methods of instant invention thereof, further experimentation is necessary to attribute a utility to C-RET and methods of its use. See Brenner v. Manson, 383 U.S. 519, 535-36, 148 USPQ 689, 696 (1966) (noting that "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing", and stated, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion."). Therefore, since C-RET is not supported by either a specific and substantial asserted utility or a well established utility, it follows that the methods of using C-RET are also not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above

Therefore, claims 23-29 remain rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility. The rejection of claims 23-29 under 35 U.S.C. 101, in paper number 16, 11/21/00 is maintained for reasons of record.

3. Applicant argues the rejection under 35 U.S.C 122, first paragraph, for lack of enablement, should be withdrawn because GDNF is a ligand that interacts with C-RET to promote tyrosine phosphorylation and a real world use for identifying such ligands is the treatment of neurodegenerative diseases such as Parkinson's disease. Applicants arguments have been fully considered but not found persuasive for the reasons given above. The specification clearly states that C-RET is an orphan receptor with no known function. There is no support in the specification nor prior art that C-RET is involved in Parkinson's disease and that ligands identified by the methods of instant invention can be used to treat said disease.

Therefore, claims 23-29 remain rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. The rejection of claims 23-29 under 35 U.S.C. 112, first paragraph, in paper number 16, 11/21/00, is maintained for reasons of record. No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nirmal Basi whose telephone number is (703) 308-9435. The examiner can normally be reached on Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for this Group is (703) 308-0294.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Nirmal S. Basi
Art Unit 1646
September 9, 2001

MICHAEL PAK
PRIMARY EXAMINER